# New Zealand Datasheet

## 1 PRODUCT NAME
Univent

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Ipratropium bromide monohydrate: 500 mcg/2 mL.
Ipratropium bromide monohydrate: 250 mcg/1 mL

## 3 PHARMACEUTICAL FORM
Inhalation ampoule: low density polyethylene single dose unit containing clear colourless to almost colourless aqueous solution.

## 4 CLINICAL PARTICULARS
### 4.1 Therapeutic indications
For the short-term acute treatment of the reversible component in chronic obstructive airways disease, such as chronic bronchitis and bronchial asthma.

### 4.2 Dose and method of administration
Adults:
The usual dose is 2 mL solution (500 mcg) nebulised and inhaled.

Children:
The usual dose is 1 mL solution (250 mcg) nebulised and inhaled.
The solution should be nebulised over 10 to 15 minutes at a gas flow of 6 to 10 L/minute.

Treatment with ipratropium bromide solution may be repeated every 4 to 6 hours as necessary.

Ipratropium bromide is commonly used in combination with a β2-agonist to maximise bronchodilation.

Recommendations for dilution of the nebuliser solution:
Under the supervision of a medical practitioner (hospital/GP surgery): solution should be diluted with preservative free sterile Sodium Chloride Inhalation Solution 0.9% to a volume of 3 to 4 mL in nebuliser bowl.

Home Use: do not dilute, unless mixed with a compatible medication described in the action plan.

### 4.3 Contraindications
Known sensitivity to atropine-like substance or inactive excipients.

### 4.4 Special warnings and precautions for use
Use of the nebuliser solution should be subject to close medical supervision during initial dosing. There have been rare reports of paradoxical bronchospasm associated with the administration of ipratropium bromide nebuliser solution. The patient should be advised to seek medical advice should a reduced response become apparent.

Generally, caution is advocated in the use of anticholinergic agents in patients with glaucoma and prostatic hypertrophy, although the risk of complications at therapeutic doses

can be considered to be minimal. Patients must be instructed in the correct administration and warned not to allow the solution or mist to enter the eyes.

## 4.5 Interaction with other medicines and other forms of interaction

Beta-adrenergics and xanthine preparations may enhance the bronchodilatory effect. Anticholinergic effects of other drugs can be intensified.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy**

As with any medicine, caution should be observed during the first trimester of pregnancy.

**Breast feeding**

Safety during lactation has not been established.

**Fertility**

Clinical data on fertility are not available for ipratropium bromide. Nonclinical studies performed with ipratropium bromide showed no adverse effect on fertility (see section 5.3).

## 4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness, accommodation disorder, mydriasis and blurred vision during treatment with Univent. If patients experience the above mentioned side effects they should avoid potentially hazardous tasks such as driving or operating machinery.

## 4.8 Undesirable effects

Anticholinergic side effects are unlikely to occur at therapeutic dosages, however, the potential for systemic adverse effects exists. Adverse effects such as dizziness, blurred vision or other changes in vision may influence the ability to drive or use machines. Some patients may complain of dryness of the mouth or notice a bitter taste. In isolated cases throat irritation or cough has been reported. There is no evidence that in the therapeutic dose range ipratropium bromide has any adverse effect on sputum viscosity or volume.

Urinary retention and constipation have only rarely been reported with ipratropium bromide.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

## 4.9 Overdose

Accidental overdose by inhalation is unlikely. Cumulative inhaled dose of up to 1.2mg produced no increase in heart rate. Single doses of ipratropium bromide of 30mg by mouth cause anticholinergic side effects but these are not severe and do not require specific reversal. However, should signs of serious anticholinergic toxicity appear, cholinesterase inhibitors may be considered.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinergics. ATC Code: R03BB01

Ipratropium bromide is a parasympathetic inhibitor used for the treatment of chronic reversible obstructive airways disease. It differs fundamentally from the sympathomimetic bronchodilators usually administered by inhalation as it blocks the vagal reflexes, which mediate bronchoconstriction. Ipratropium bromide exerts a local effect on the airways and has a high therapeutic ratio, producing bronchodilation without significant effect on other body systems. Ipratropium bromide is, therefore, very well tolerated and is suitable for use in patients with cardiac or circulatory disorders, thyrotoxicosis and for those patients unacceptably sensitive to, or unresponsive to other bronchodilators.

The onset of action occurs 3-5 minutes after inhalation and the effect on the airways lasts for 5-6 hours.

## 5.2 Pharmacokinetic properties

The systemic bioavailability after inhalation is very low. As compared with intravenous and oral administration, it amounts to only 5% and 10-30%, respectively. Plasma level behaviour after inhalation is similar to that after oral use. Following inhalation of 0.555mg, the peak plasma concentrations were only 0.06 ng/ml after 3 hours.

The elimination half-life (active ingredient and metabolites) is about 3-4 hours. Renal elimination after intravenous use amounts to about 70% of the labelled dose administered, partly in the form of inactive metabolites. Serum protein binding is less than 20%. There is no transgression of the blood/brain barrier.

## 5.3 Preclinical safety data

The toxicity of ipratropium bromide has been investigated extensively in the following types of studies: acute, subchronic and chronic toxicity, carcinogenicity, reproductive toxicity and mutagenicity via oral, intravenous, subcutaneous, intranasal and/or inhalation routes. Based on these toxicity studies, the probability of systemic anticholinergic side effects decreases in the following order:

intravenous > subcutaneous > oral > inhalation > intranasal.

Pre-clinically, ipratropium bromide was found to be well-tolerated. Two-year carcinogenicity studies in rats and mice have revealed no carcinogenic activity at doses up to approximately 1,200 times the maximum recommended human daily dose for intranasal ipratropium. Results of various mutagenicity tests were negative.

Studies to investigate the possible influence of ipratropium bromide on fertility, embryo-fetotoxicity, and peri-/postnatal development have been performed on mice, rats and rabbits. High oral levels, i.e. 1000 mg/kg/day in the rat and 125 mg/kg/day in the rabbit were maternotoxic for both species and embryo-/fetotoxic in the rat, where the fetal weight was reduced. Treatment-related malformations were not observed. The highest, technically feasible doses for inhalation of the pressurised inhalation, solution, 1.5 mg/kg/day (human equivalent dose of 0.24 mg/kg/day) in rats and 1.8 mg/kg/day (human equivalent dose of 0.576 mg/kg/day) in rabbits, showed no adverse effects on reproduction.

These doses are 6- and 14-fold the maximum recommended human daily dose (MRHDD) of 2 mg or 0.04 mg/kg (based on a body weight of 50 kg).

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Excipients include sodium chloride, hydrochloric acid and purified water.

## 6.2 Incompatibilities
Not applicable.

## 6.3 Shelf life
Shelf life is 24 months (2 years) from manufacture.

## 6.4 Special precautions for storage
Store below 25°C. Protect from light.

This product contains no preservative. A fresh dose unit should be used for each dose which should be opened immediately before administration. Any remaining solution should be discarded.

## 6.5 Nature and contents of container
Cartons of 20 inhalation ampoules.

## 6.6 Special precautions for disposal
None.

# 7 MEDICINE SCHEDULE
Prescription Medicine.

# 8 SPONSOR
Rex Medical Ltd
PO Box 18-119
Glen Innes
AUCKLAND.
Ph (09) 574 6060
Fax (09) 574 6070

# 9 DATE OF FIRST APPROVAL
5 April 2007

# 10 DATE OF REVISION OF THE TEXT
14 September 2018

## SUMMARY TABLE OF CHANGES

| Section changed | Summary of new information |
|---|---|
| 4.6 | Fertility section added |
| 4.7 | Section added |
| 4.8 | Reporting of adverse events added |
| 4.9 | Poison information centre contact added |
| 5.3 | Section added |